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THE TOXICITY OF CERTAIN ORGANIC COMPOUNDS
TO YOUNG SCREWWORM LARVAE

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The research program at the Menard, Tex., station includes the laboratory testing of materials for possible use as wound dressings to prevent infestation by larvae of the screwworm (Cochliomyia americana C. and P.). The method of testing and the results obtained with a large number of organic compounds have been reported by Bushland (1940a and b). The results obtained with 126 additional compounds supplied by the Division of Insecticide Investigations are presented in this paper.

As in the previous experiments, the desired amount of finely ground test material was mixed thoroughly with ground lean beef, bovine blood, water, and sufficient formaldehyde to retard putrefaction. Approximately 100 newly hatched larvae were placed on 150 grams of this treated medium in an uncovered wide-mouth pint Mason jar. The test jars were held at a temperature favorable for larval growth, and daily observations were made over a period of 3 days. The percentage mortality was then estimated, and any abnormalities in the surviving larvae were noted.

The larvae used in these tests were from the same inbred stock used in the work published by Bushland (1940a). Similar care was given in maintaining this stock to obtain uniform test larvae.

In these tests 0.25 gram of test material per jar (concentration 0.17 percent) was generally studied first. If all larvae were killed, in subsequent tests the dosage was reduced until some larvae survived. If all larvae were not killed at 0.25 gram per jar, the dosage was increased up to a maximum of 1.0 gram per jar (concentration 0.67 percent). All tests except those at the 1.0-gram dosage were conducted in duplicate, and with every lot of larvae four check jars were run. For these gross toxicity determinations it was not considered necessary to repeat tests, since experience had indicated that the results could generally be duplicated, and with toxic substances the results at dosages above and below the minimum lethal dosage served to confirm the observations.

The results of these tests are summarized in table 1. The various compounds are grouped according to their chemical classification. Two lethal concentrations are given, the highest concentration at which some larvae survived and the lowest concentration that caused 100 percent mortality (minimum lethal concentration) within the 3-day observation period. Materials described as slightly toxic are those failing to kill all larvae but causing some mortality or retardation in larval growth at a dosage of 1.0 gram per jar. Those compounds producing no noticeable ill effects at this dosage are designated as nontoxic.

Table 1.--Toxicity of various organic compounds against young screwworm larvae

Compound	: Highest concen- tration at which larvae survived :	Percent	Percent
Azo, hydrazo, and related compounds:			
p-Bromohydrazobenzene <chem>BrC6H4NNHC6H5</chem>	0.05	0.08	
p-Ethoxyazobenzene <chem>C6H5NNC6H4OC2H5</chem>	.05	.08	
p-Ethoxyhydrazobenzene <chem>C6H5NNHC6H4OC2H5</chem>	.08	.10	
9-Fluorenonephenylhydrazone <chem>C6H4C(NNHC6H5)C6H4</chem>		Nontoxic	
p-Iodoazobenzene <chem>C6H5NNHC6H4I</chem>	.10	.17	
p-Methylazobenzene <chem>C6H5NNC6H4CH3</chem>	.05	.08	
p-Methylhydrazobenzene <chem>C6H5NNHC6H4CH3</chem>	.08	.10	
Heterocyclic compounds with sulfur outside ring:			
Piperidine-piperidyl dithiocarbamate <chem>(C5H10N)C(S)SH(C5H11N)</chem>		.17	.34
Thiocoumarin <chem>C6H4CH=CHC(S)O</chem>		Less than .03	

Table 1 (Continued)

Compound	: Highest : : concen- : Minimum : tration : lethal : at which : concen- : larvae : tration : survived :		
	Percent	Percent	
Heterocyclic compounds with 5-membered rings not containing sulfur:			
N-Benzylpyromucamide (C ₄ H ₃ O)CONHCH ₂ C ₆ H ₅	0.05	0.08	
N-Cyclohexylpyromucamide (C ₄ H ₃ O)CONHC ₆ H ₁₁	.05	.10	
9-Furalfluorene <u>C₆H₄C</u> [CH(C ₄ H ₃ O)] C ₆ H ₄	.17	.67	
2-Furanacrylamide (C ₄ H ₃ O)CONH ₂	.03	.05	
beta-Furfuraldoxime (C ₄ H ₃ O)CH(NO _H)	.10	.17	
Phenazine oxide <u>C₆H₄NONC</u> C ₆ H ₄	.01	.03	
1,2,3,4-Tetrahydrocarbazole <u>C₆H₄NHC</u> C ₆ H ₈	.17	.67	
N-p-Tolylpyromucamide (C ₄ H ₃ O)CONHC ₆ H ₄ CH ₃	.08	.10	
N-Xenylpyromucamide (C ₄ H ₃ O)CONHC ₆ H ₄ C ₆ H ₅			Nontoxic
N-(2,4-Xylyl)pyromucamide (C ₄ H ₃ O)CONHC ₆ H ₃ (CH ₃) ₂	.10	.17	

Table 1 (Continued)

Compound	: Highest : : concen- : Minimum : tration : lethal : at which : concen- : larvae : tration : survived :				
	<u>Percent</u>	<u>Percent</u>			
N-(2,5-Xylyl)pyromucamide (C ₄ H ₃ O)CONHC ₆ H ₃ (CH ₃) ₂	0.17	0.34			
N-(2,6-Xylyl)pyromucamide (C ₄ H ₃ O)CONHC ₆ H ₃ (CH ₃) ₂	.03	.05			
Heterocyclic compounds with 6-membered rings not containing sulfur:					
3-Acetyl-6-methyl-1,2-pyran-2, 4(3)dione (dehydroacetic acid) <u>OCCHC(CH₃)OC(O)CHCOCH₃</u>	.05	.10			
2-Chloroacridone <u>C₆H₄COCl₆H₃C1NH</u>	Nontoxic				
4-Chloroacridone <u>C₆H₄COCl₆H₃C1NH</u>	Nontoxic				
2,3-Dihydroquinidine-12-carboxylic acid <u>C₆H₄C(CO₂H)C(CH₂)₃C=N</u>	.17	.67			
4-(2,4-Dinitrophenyl)morpholine (NO ₂) ₂ C ₆ H ₃ N(CH ₂ CH ₂) ₂ O	Nontoxic				
Dipiperonal cyclopentanone <u>OCH₂OC₆H₃CHCC(O)C(CHC₆H₃OCH₂O)CH₂CH₂</u>	.17	.67			
4-Hydroxyacridone <u>C₆H₄COCl₆H₃(OH)NH</u>	.17	.67			

Table 1 (Continued)

Compound		
	: Highest : : concen- : Minimum : tration : lethal : at which : concen- : larvae : tration : survived :	
	<u>Percent</u>	<u>Percent</u>
Morpholine $\underline{\text{NH}(\text{CH}_2)_2\text{O}(\text{CH}_2)_2}$	0.10	0.17
4-(4-Nitrophenyl)morpholine $\text{NO}_2\text{C}_6\text{H}_4\text{N}(\text{CH}_2\text{CH}_2)_2\text{O}$		Nontoxic
2,2,6,6-Tetramethyl-1-nitroso-4-piperidone $(\text{CH}_3)_2\underline{\text{CCH}_2\text{COCH}_2\text{C}(\text{CH}_3)_2}\text{NNO}$.17	.67
Xanthene $\underline{\text{C}_6\text{H}_4\text{CH}_2\text{C}_6\text{H}_4\text{O}}$		Less than .03
Xanthydrol $\underline{\text{C}_6\text{H}_4\text{CH}(\text{OH})\text{C}_6\text{H}_4\text{O}}$.03	.05
Thiocyanato compounds:		
p-Thiocyanobromobenzene $\text{BrC}_6\text{H}_4\text{SCN}$.05	.10
p-Thiocyaniodobenzene $\text{IC}_6\text{H}_4\text{SCN}$.10	.17
Amines, amides, imines, and imides containing sulfur:		
p-Aacetamino-N-m-nitrophenylbenzene sulfonamide $\text{CH}_3\text{CONHC}_6\text{H}_4\text{SO}_2\text{NHC}_6\text{H}_4\text{NO}_2$		Nontoxic
p-Aacetamino-N-o-nitrophenylbenzene sulfonamide $\text{CH}_3\text{CONHC}_6\text{H}_4\text{SO}_2\text{NHC}_6\text{H}_4\text{NO}_2$		Nontoxic

Table 1 (Continued)

Compound	: Highest concen- tration at which larvae survived :	: Minimum lethal concen- tration
	<u>Percent</u>	<u>Percent</u>
p-Bromobenzenesulfonamide <chem>BrC6H4SO2NH2</chem>	0.01	0.03
p-Chlorobenzenesulfonamide <chem>ClC6H4SO2NH</chem>	.01	.03
Dithiooxamide <chem>NH2C(S)C(S)NH2</chem>	.08	.10
m-Nitrobenzenesulfonamide <chem>NO2C6H4SO2NH2</chem>	.03	.05
m-Nitro-N-phenylbenzenesulfonamide <chem>NO2C6H4SO2NHC6H5</chem>		Nontoxic
3-Nitro-4-toluenesulfonamide <chem>CH3C6H3(NO2)SO2NH2</chem>	.10	.17
p-Toluenesulfonamide <chem>CH3C6H4SO2NH2</chem>	.10	.17
Sulfides, disulfides, and mercaptans:		
n-Butyl sulfone <chem>(C4H9)2SO2</chem>	.05	.08
Thio-2-naphthylmethyl ether <chem>C10H7SCH3</chem>	.10	.17
Aldehydes, ketones, thicaldehydes, and thioketones:		
Acenaphthylphenyl ketone <chem>C6H5COC10H5(CH2)2</chem>		Nontoxic

Table 1 (Continued)

Compound	: Highest : : concen- : Minimum : tration : lethal : at which : concen- : larvae : tration : survived :		
	Percent	Percent	
Dianisalicyclopentanone $(\text{CH}_3\text{OC}_6\text{H}_4\text{CH})_2\text{CCH}_2\text{CH}_2\text{CCO}$			Slightly toxic
Dibenzalicyclopentanone $\text{C}_6\text{H}_5\text{CH}=\text{CCH}_2\text{CH}_2\text{C}(=\text{CHC}_6\text{H}_5)\text{CO}$			Nontoxic
alpha, alpha-Dichloro-p-phenylacetophenone $\text{C}_6\text{H}_5\text{C}_6\text{H}_4\text{COCHCl}_2$	0.10	0.17	
2-Fluorophenyl ketone $\text{C}_{13}\text{H}_9\text{COC}_6\text{H}_5$			Nontoxic
p-Methylacetophenone $\text{CH}_3\text{C}_6\text{H}_4\text{COCH}_3$.10	.17	
2-Nitrophenanthraquinone $\text{C}_6\text{H}_4\text{COCOC}_6\text{H}_3\text{NO}_2$			Nontoxic
2,3-Octanedione-3-oxime $\text{CH}_3(\text{CH}_2)_4\text{C}(\text{NOH})\text{COCH}_3$			Slightly toxic
Phenylglyoxal oxime $\text{C}_6\text{H}_5\text{COCHNOH}$.10	.17	
1-Phenyl-1,2-propanedione-2-monoxime $\text{C}_6\text{H}_5\text{COC}(\text{NOH})\text{CH}_2\text{CH}_3$			Nontoxic
2,6,7-Trinitrofluorenone $(\text{NO}_2)_2\text{C}_6\text{H}_2\text{COC}_6\text{H}_3\text{NO}_2$			Nontoxic

Table 1 (Continued)

Compound	: Highest : : concen- : Minimum : tration : lethal : at which : concen- : larvae : tration : survived :	<u>Percent</u>	<u>Percent</u>
Phenols and phenol ethers:			
beta, beta'-Dinaphthol $\text{HO-C}_{10}\text{H}_6\text{C}_{10}\text{H}_6\text{OH}$			Nontoxic
3-Hydroxy-4-nitro-2-naphthoic acid $\text{C}_{10}\text{H}_5(\text{NO}_2)(\text{OH})\text{COOH}$		0.17	0.67
2-Nitroso-1-naphthol $\text{C}_{10}\text{H}_6(\text{NO})\text{OH}$			Slightly toxic
Quinhydrone $\text{C}_6\text{H}_4\text{O}_2\text{C}_6\text{H}_4(\text{OH})_2$.17	.67
Amines, amides, imines, and imides not containing sulfur:			
Acetoacetic acid ethyl ester semicarbazone $\text{CH}_3\text{C}(\text{NNHCNH}_2)\text{CH}_2\text{COOC}_2\text{H}_5$			Slightly toxic
Acetonyl acetone disemicarbazone $[\text{CH}_3\text{C}(\text{NNHCNH}_2)_2\text{CH}_2]_2$			Slightly toxic
Acetophenone semicarbazone $\text{C}_6\text{H}_5\text{C}(\text{NNHCNH}_2)\text{CH}_3$.05	.10
alpha-Anisaldoxime $\text{CH}_3\text{OC}_6\text{H}_4\text{CH=NOH}$.10	.17
Benzaldehyde semicarbazone $\text{C}_6\text{H}_5\text{CHNNHCNH}_2$			Slightly toxic
Benzoin semicarbazone $\text{C}_6\text{H}_5\text{CH}(\text{OH})\text{C}(\text{NNHCNH}_2)\text{C}_6\text{H}_5$			Nontoxic

Table 1 (Continued)

Compound	: Highest : : concen- : Minimum : tration : lethal : at which : concen- : larvae : tration : survived :	<u>Percent</u>	<u>Percent</u>
Benzophenone semicarbazone $(C_6H_5)_2CNNHCNH_2$		0.01	0.03
N-Carvacrylpalmitamide $C_{15}H_{31}CONHC_6H_3(CH_3)(C_3H_7)$		Nontoxic	
Carvacrylpropionamide $C_2H_5CONHC_6H_3(CH_3)(C_3H_7)$		Nontoxic	
omega-Chloroacetanilide $C_6H_5NHCOCH_2Cl$		Less than .03	
p-Chloroacetophenone semicarbazone $C_1C_6H_4C(CH_3)NNHCNH_2$		Nontoxic	
Cinnamaldehyde semicarbazone $C_6H_5CHCHCHNNHCNH_2$		Nontoxic	
Crotonaldehyde semicarbazone $CH_3CHCHCHNNHCNH_2$.05	.10
alpha-Cyanoacetanilide $CNCH_2CONHC_6H_5$		Slightly toxic	0.34
Cyclopentanone semicarbazone $C_5H_8(NNHCONH_2)$.10	.17
Dibutylamine $(C_4H_9)_2NH$.03	.08
2,6-Dimethyl-4-heptanone semi- carbazone $[(CH_3)_2CHCH_2]_2CNNHCNH_2$.01	.03

Table 1 (Continued)

Compound	: Highest : : concen- : Minimum : tration : lethal : at which : concen- : larvae : tration : survived :		
	Percent	Percent	
Ethylmethyl ketone semicarbazone $C_2H_5C(NNHCONH_2)CH_3$	0.10	0.17	
alpha-Ethylbutyraldehyde semi- carbazone $(C_2H_5)_2CHCHNNHCONH_2$.34	.67	
9-Fluorenone oxime $C_6H_4C(NOH)C_6H_4$			Nontoxic
Fluorylaniline $C_6H_4CH_2C_6H_3NH_2$.34	.67	
2-Furaldehyde semicarbazone $(C_4H_3O)CHNNHCONH_2$.05	.10	
p-Methylacetophenone semicarbazone $CH_3C_6H_4C(CH_3)NNHCOC_6H_5$			Nontoxic
N-Methyl-m-acetotoluide $CH_3CON(CH_3)C_6H_4CH_3$.10	.17	
4'-Methyl-4-nitrodiphenylamine $CH_3C_6H_4NHC_6H_4NO_2$			Nontoxic
4-Methyl-2-pentanone semicarbazone $(CH_3)_2CHCH_2C(CH_3)NNHCONH_2$.17	.34	
Methylpropyl ketone semicarbazone $CH_3C(NNHCONH_2)C_3H_7$.10	.17	
p-Nitrosodiethylaniline $(C_2H_5)_2NC_6H_4NO$.08	.10	
2-Octanone semicarbazone $CH_3(CH_2)_5C(CH_3)NNHCONH_2$			Slightly toxic

Table 1 (Continued)

Compound	: Highest concen- tration at which larvae survived :	Percent	Percent
	Minimum lethal concen- tration :		
Phthalonitrile $C_6H_4(CN)_2$		0.03	0.05
Salicylaldehyde semicarbazone $HOC_6H_4CHNNHCONH_2$			Nontoxic
2,4,2',4'-Tetrabromodiphenylamine $Br_2C_6H_3NHC_6H_3Br_2$			Nontoxic
2,4,2',4'-Tetrachlorodiphenylamine $Cl_2C_6H_3NHC_6H_3Cl_2$			Nontoxic
p-Tollylacetamide $CH_3CHOHCONHC_6H_4CH_3$.17	.67
Bis-(2,4,6-trinitrophenyl)amine $[(NO_2)_3C_6H_2]_2NH$			Less than .03
N-Xenylacetamide $CH_3CONHC_6H_4C_6H_5$			Slightly toxic
N-Xenylbenzamide $C_6H_5CONHC_6H_4C_6H_5$			Nontoxic
N-Xenylformamide $HCONHC_6H_4C_6H_5$			Nontoxic
N-Xenylpropionamide $C_2H_5CONHC_6H_4C_6H_5$			Nontoxic
N-(2,4-Xylyl)benzamide $C_6H_5CONHC_6H_3(CH_3)_2$			Nontoxic

Table 1 (Continued)

Compound	: Highest : concen- : Minimum tration : lethal at which : concen- larvae : tration survived :	<u>Percent</u>	
		<u>Percent</u>	<u>Percent</u>
N-(2,5-Xylyl)benzamide $C_6H_5CONHC_6H_3(CH_3)_2$			Nontoxic
N-(2,6-Xylyl)benzamide $C_6H_5CONHC_6H_3(CH_3)_2$			Nontoxic
N-(2,4-Xylyl)formamide $HCONHC_6H_3(CH_3)_2$		0.10	0.17
N-(2,5-Xylyl)formamide $HCONHC_6H_3(CH_3)_2$.05	.10
N-(2,6-Xylyl)formamide $HCONHC_6H_3(CH_3)_2$.05	.10
N-(2,4-Xylyl)propionamide $C_2H_5CONHC_6H_3(CH_3)_2$			Slightly toxic
N-(2,5-Xylyl)propionamide $C_2H_5CONHC_6H_3(CH_3)_2$			Nontoxic
N-(2,6-Xylyl)propionamide $C_2H_5CONHC_6H_3(CH_3)_2$.17	.34
Acids, alcohols, and esters:			
2-Acetoxy-2-naphthoic acid $CH_3COOC_{10}H_6COOH$.17	.67
2,4-Dinitrophenol acetate $CH_3CO_2C_6H_3(NO_2)_2$.05	.10
9-Fluorenol acetate $C_6H_4CH(OCOCH_3)C_6H_4$			Nontoxic

Table 1 (Continued)

Compound	: Highest concentration at which larvae survived :	: Minimum lethal concentration : concen- tration : survived :
	<u>Percent</u>	<u>Percent</u>
p-Nitroiodosobenzene acetate $(NO_2)C_6H_4I=(OCOCH_3)_2$		Nontoxic
Nitro and nitroso compounds:		
alpha, beta-Dibromo-beta-nitroethylbenzene $C_6H_5CHBrCHBrNO_2$	0.05	0.08
o-Iodosonitrobenzene $C_6H_4(NO_2)IO$.05	.08
l-Nitronaphthalene $C_{10}H_7NO_2$.05	.08
o-Nitronitrosobenzene $NO_2C_6H_4NO$		Nontoxic
beta-Nitrosostyrene $C_6H_5CH=CHNO$.10	.17
4-Nitrosothymol $(CH_3)_2CHC_6H_2(CH_3)(OH)NO$		Nontoxic
2,4,6-Trinitrotoluene $C_6H_2(CH_3)(NO_2)_3$.08	.10
Aryl, alkyl, and aralkyl halides:		
3-Bromoacenaphthene $C_{10}H_5(CH_2)_2Br$.17	.67
2-Bromofluorene $\underline{C_6H_4CH_2C_6H_3Br}$.05	.08

Table 1 (Continued)

Compound	: Highest : : concen- : Minimum : tration : lethal : at which : concen- : larvae : tration : survived :		
	<u>Percent</u>	<u>Percent</u>	
9-Chlorofluorene <u>C₆H₄CHClC₆H₄</u>			Nontoxic
1-Chloronaphthalene <u>C₁₀H₇Cl</u>	0.10	0.17	
Iodosobenzene <u>C₆H₅IO</u>	.10	.17	
2-Iodofluorene <u>C₆H₄CH₂C₆H₃I</u>			Nontoxic

Materials that were found to be at least as toxic as diphenylamine 1/ are tabulated below. Compounds of similar effectiveness

1/ Bushland (1940a) reported that the minimum lethal concentration for diphenylamine was 0.10-0.17 percent (all larvae killed at 0.17 but some survived at 0.10 percent). Melvin and coworkers (1939a and b, 1941) have shown that diphenylamine is a practical screwworm remedy. Although in laboratory tests many compounds have been effective at lower dosages than are required for diphenylamine, field tests evaluating such qualities as duration of protection, toxicity to infested animals, and rate of healing of treated wounds have shown that the diphenylamine treatment is preferable to any others so far considered.

are listed alphabetically within groups, and the groups are arranged in decreasing order of toxicity.

Killed all larvae at a concentration of 0.03 percent:

Benzophenone semicarbazone

Bis-(2,4,6-trinitrophenyl)amine

p-Bromobenzenesulfonamide

omega-Chloroacetanilide

p-Chlorobenzenesulfonamide

2,6-Dimethyl-4-heptanone semicarbazone

Phenazine oxide

Thiocoumarin

Xanthene

Killed all larvae at a concentration of 0.05 percent but some survived

at 0.03 percent:

2-Furanacrylamide

m-Nitrobenzenesulfonamide

Phthalonitrile

Xanthydrol

N-(2,6-Xylyl)pyromucamide

Killed all larvae at 0.10 percent but some survived at 0.05 percent:

Acetophenone semicarbazone

3-Acetyl-6-methyl-1,2-pyran-2,4(3)-dione

(dehydroacetic acid)

N-Benzylpyromucamide

2-Bromofluorene

p-Bromohydrazobenzene

n-Butyl sulfone

Crotonaldehyde semicarbazone

alpha, beta-Dibromo-beta-nitroethylbenzene

Dibutylamine

2,4-Dinitrophenol acetate

Dithioxamide

p-Ethoxyazobenzene

p-Ethoxyhydrazobenzene

2-Furaldehyde semicarbazone

o-Iodosonitrobenzene

p-Methylazobenzene

p-Methylhydrazobenzene

1-Nitronaphthalene

p-Nitrosodiethylaniline

p-Thiocyanobromobenzene

N-p-Tolylpyromucamide

2,4,6-Trinitrotoluene

N-(2,5-Xylyl)formamide

N-(2,6-Xylyl)formamide

Killed all larvae at 0.10 percent but some survived at 0.17 percent:

alpha-Anisaldoxime

1-Chloronaphthalene

Cyclopentanone semicarbazone

alpha, alpha-Dichloro-p-phenylacetophenone

Ethylmethyl ketone semicarbazone

beta-Furfuraldoxime

p-Iodoxydrazobenzene

Iodosobenzene

p-Methylacetophenone

N-Methyl-m-acetotoluide

Methylpropyl ketone semicarbazone

Morpholine

beta-Nitrosostyrene

3-Nitro-4-toluenesulfonamide

Phenylglyoxal oxime

p-Thiocyaniodobenzene

Thio-2-naphthylmethyl ether

p-Toluenesulfonamide

N-(2,4-Xylyl)formamide

N-(2,4-Xylyl)pyromucamide

SUMMARY

As a means of selecting larvicidal materials effective against the screwworm, 126 organic compounds were tested in the laboratory by the jar method. In these tests 37 compounds were more toxic than diphenylamine and 20 compounds were of about the same toxicity. Toxic materials were found in all 13 classes of organic compounds tested, and 40 nontoxic materials were present in 10 classes.

Newly hatched screwworm larvae failed to survive for 3 days when their food contained as much as 0.03 percent of any of the following compounds: bis-(2,4,6-Trinitrophenylamine), p-bromobenzenesulfonamide, omega-chloroacetanilide, p-chlorobenzenesulfonamide, 2,6-dimethyl-4-heptanone semicarbazone, phenazine oxide, thiocoumarin, and xanthene.

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